

## PATENT COOPERATION TREATY

**PCT**  
**NOTIFICATION OF TRANSMITTAL**  
**OF COPIES OF TRANSLATION**  
**OF THE INTERNATIONAL PRELIMINARY**  
**EXAMINATION REPORT**

(PCT Rule 72.2)

From the INTERNATIONAL BUREAU

To:

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Date of mailing (day/month/year) 20 February 2004 (20.02.04)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference P2710PCT-AJ	
International application No. PCT/JP02/06260	International filing date (day/month/year) 24 June 2002 (24.06.02)
Applicant AJINOMOTO CO., INC. et al	

**1. Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

**2. Transmittal of the copy of the translation to the elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

EP,CA,CN,KP,RO,US

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AP,EA,AE,AG,AL,AM,AT,AU,AZ,BA,BB,BG,BR,BY,BZ,CH,CO,CR,CU,CZ,DE,DK,DM,DZ,EC,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KR,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,MZ,NO,NZ,OM,PH,PL,PT,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TN,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZM,ZW,OA

**3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

**It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.**

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Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P2710PCT-AJ	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP02/06260	International filing date (day/month/year) 24 June 2002 (24.06.02)	Priority date (day/month/year) 25 June 2001 (25.06.01)
International Patent Classification (IPC) or national classification and IPC A61K 45/08, A61P 35/00		
Applicant AJINOMOTO CO., INC.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of _____ sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 25 December 2002 (25.12.02)	Date of completion of this report 03 June 2003 (03.06.2003)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP02/06260

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☐ the description:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the claims:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, as amended (together with any statement under Article 19  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

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## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 13-17

because:

- ☒ the said international application, or the said claims Nos. 13-17 relate to the following subject matter which does not require an international preliminary examination (*specify*):

See supplemental sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 13-17

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

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**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III. 1.

The inventions set forth in Claims 13-17 pertain to  
"methods for treatment of the human body by therapy" (PCT  
Rule 67.1(iv)).

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2, 7-8	YES
	Claims	1, 3, -6, 9-12, 18	NO
Inventive step (IS)	Claims		YES
	Claims	1-12, 18	NO
Industrial applicability (IA)	Claims	1-12, 18	YES
	Claims		NO

2. Citations and explanations

The following documents are cited in the international search report.

- Document 1: WO 98/32440 A1 (The Proctor & Gamble Co.)
- Document 2: WO 97/05870 A2 (The Proctor & Gamble Co.)
- Document 3: WO 99/51246 A (Ajinomoto Co., Inc.)
- Document 4: B. Raymond et al., "Hypersensitivity reactions from taxol", Journal of Clinical Oncology (1990), Vol. 8, No. 7, pp. 1263-1268
- Document 5: S. Eckhardt et al., "The effect of docetaxel on malignant tumors", Orvosi Hetilap (1998), Vol. 139, No. 15, pp. 867-872
- Document 6: George P. Browman et al., "Modified adriamycin-vincristine-dexamethasone (m-VAD) in primary and relapsed plasma cell myeloma: an NCI (Canada) pilot study", British Journal of Haematology (1992), Vol. 82, pp. 555-559

Document 1 discloses substances with tubulin polymerization inhibiting activity and adreno-corticosteroids as chemotherapeutic agents for combating tumour activity, and mentions that corticosteroids are

used for their antiinflammatory action as well as their capacity to inhibit mitosis and stop DNA synthesis, with dexamethasone, prednisolone and methylprednisolone being such compounds.

Document 2 discloses substances with tubulin polymerization inhibiting activity and adreno-corticosteroids as chemotherapeutic agents having anti-tumour activity, and mentions that corticosteroids are used for their antiinflammatory action as well as their capacity to inhibit mitosis and stop DNA synthesis, with dexamethasone, prednisolone and methylprednisolone being such compounds.

Document 3 discloses stilbene and the derivative thereof (Z)-N-[2-methoxy-[2-(3,4,5-trimethoxyphenyl)-vinyl]phenyl]-L-serinamide as substances having tubulin polymerization inhibiting activity.

Document 4 discloses combined use of taxol - i.e. a substance with tubulin polymerization inhibiting activity - and a corticosteroid - i.e. a steroidal substance having antiinflammatory activity (see page 1265, lines 11-13).

Document 5 discloses use of docetaxel- i.e. a substance with tubulin polymerization inhibiting activity - in combination with a steroid - i.e. a substance having antiinflammatory activity - in order to mitigate the toxicity thereof.

Document 6 discloses combined use of vincristine - i.e. a substance with tubulin polymerization inhibiting activity - in combination of with dexamethasone - i.e. a substance having antiinflammatory activity - for the treatment of myelomas.

- Novelty and inventive step of Claims 1, 3-6, 9-12 and

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Documents 1 and 2 do not disclose combined use of a substance with tubulin polymerization inhibiting activity

and a steroidal substance with antiinflammatory activity. However, combined use of a plurality of chemotherapeutic agents for the treatment of cancer is obvious to a person skilled in the art.

Therefore, the inventions set forth in the above claims are not novel and do not involve an inventive step in the light of Document 1 or 2.

The inventions set forth in the above claims are also not novel and do not involve an inventive step in the light of Documents 4, 5 and 6.

- Novelty and inventive step of Claims 2 and 7-8

The inventions set forth in the above claims differ from Documents 1, 2, 4, 5 and 6 in that a stilbene derivative, and more especially (Z)-N-[2-methoxy-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide, is used as the substance with tubulin polymerization inhibiting activity. However, aforementioned compounds are known from the disclosure in Document 3 to be substances with tubulin polymerization inhibiting activity. Therefore use of a stilbene derivative, and more especially (Z)-N-[2-methoxy-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide, instead of the other substances with tubulin polymerization inhibiting activity in the inventions disclosed in Documents 1, 2, 4, 5 and 6 is obvious to a person skilled in the art.

Therefore, the inventions set forth in the above claims are novel, but they do not involve an inventive step in the light of Documents 1-6.